A

```
1     TGAAATATAGGTGAGAGACAAGATTGTCTCATATCCGGGGAAATCATAACCTATGACTAG
61    GACGGGAAGAGGAAGCACTGCCTTTACTTCAGTGGGAATCTCGGCCTCAGCCTGCAAGCC
121   AAGTGTTCACAGTGAGAAAAGCAAGAGAATAAGCTAATACTCCTGTCCTGAACAAGGCAG
181   CGGCTCCTTGGTAAAGCTACTCCTTGATCGATCCTTTGCACCGGATTGTTCAAAGTGGAC
241   CCCAGGGGAGAAGTCGGAGCAAAGAACTTACCACCAAGCAGTCCAAGAGGCCCAGAAGCA
301   AACCTGGAGGTGAGACCCAAAGAAAGCTGGAACCATGCTGACTTTGTACACTGTGAGGAC
          L  E  V  R  P  K  E  S  W  N  H  A  D  F  V  H  C  E  D  19
361   ACAGAGTCTGTTCCTGGAAAGCCCAGTGTCAACGCAGATGAGGAAGTCGGAGGTCCCCAA
       T  E  S  V  P  G  K  P  S  V  N  A  D  E  E  V  G  G  P  Q  39
421   ATCTGCCGTGTATGTGGGGACAAGGCCACTGGCTATCACTTCAATGTCATGACATGTGAA
       I  C  R  V  C  G  D  K  A  T  G  Y  H  F  N  V  M  T  C  E  59
481   GGATGCAAGGGCTTTTTCAGGAGGGCCATGAAACGCAACGCCCGGCTGAGGTGCCCCTTC
       G  C  K  G  F  F  R  R  A  M  K  R  N  A  R  L  R  C  P  F  79
541   CGGAAGGGCGCCTGCGAGATCACCCGGAAGACCCGGCGACAGTGCCAGGCCTGCCGCCTG
       R  K  G  A  C  E  I  T  R  K  T  R  R  Q  C  Q  A  C  P  L  99
601   CGCAAGTGCCTGGAGAGCGGCATGAAGAAGGAGATGATCATGTCCGACGAGGCGCTGGAG
       R  K  C  L  E  S  G  M  K  K  E  M  I  M  S  D  E  A  V  E  119
661   GAGAGGCGGGCCTTGATCAAGCGGAAGAAAAGTGAACGGACAGGGACTCAGCCACTGGGA
       E  R  R  A  L  I  K  R  K  K  S  E  R  T  G  T  Q  P  L  G  139
721   GTGCAGGGGCTGACAGAGGAGCAGCGGATGATGATCAGGGAGCTGATGACGCTGAGAATG
       V  Q  G  L  T  E  E  Q  R  M  M  I  R  E  L  M  T  L  R  M  159
781   AAAACTTTTGACACTAGCTTTCTGCATTTCAAGAATTTCCGGCTGCCAAGGGTTCTTCAA
       K  T  F  D  T  S  F  L  H  F  K  N  F  R  L  P  R  V  L  S  179
841   AGTGGCTCTTCAATTTGTCAACAAGTCTTCTGCAGGCCCCATCGACTGAAAAAACTCTTAA
       S  G  L  Q  L  P  E  C  L  D  A  P  I  R  L  E  A  A  P  N  199
901   AGCCAGGTTCCCAAAGATCTGTGCTGTTTGAAGGTCTCTCTGCAGCTGCCCCGGGAGAT
       S  Q  V  P  F  D  L  C  S  L  K  V  S  L  Q  L  P  G  E  D  219
961   GCTAGTGTCTTGGAACTACAAACTCCCAGCCGACAGTGGCGGGAAAGACATCTTCTTCTG
       G  S  V  W  N  Y  K  P  P  A  D  S  G  G  K  E  I  F  F  L  239
1021  CTGCTCGACATGCTGACATGTCAACGTACATGTTCAAAGGCATCATCAGCTTTTCTAAA
       L  P  H  M  A  D  M  S  T  Y  M  F  K  G  I  I  S  F  A  F  259
1081  GTCATCTCGTACTTCAGGGACTTGCCCATCGAGGACCAGATCTCGCTGCTGAAGGGGGC
       V  I  S  Y  F  R  D  L  P  I  E  D  Q  I  S  L  L  K  G  A  279
1141  GCTTTCGAGCTGTGTCAACTGAGATTCAACACAGTGTTCAACGGCGAGACGTGGAA
       A  F  E  L  C  Q  L  R  F  N  T  V  F  N  A  E  T  G  T  W  299
1201  GAGTGTGGCCGGGCTGTCGTACTGCTTGGAAGACACTGCAGGTGGCTTCGAGCAACTTCA
       E  C  G  R  L  S  Y  C  L  E  D  T  A  G  G  F  Q  Q  L  L  319
1261  CTGGAGTCCATCTCTGAAATTCCACTACATGCTGAAGAAGTTGCAGCTTCATGAGGAGGAG
       L  E  P  M  L  K  F  H  Y  M  L  K  K  L  Q  L  H  E  E  E  339
1321  TATGTGCTGATGCAGGCTATTGCGCTGTTCTCCCCGAGACGGCGCAGATGTGGTTCAAAAA
       Y  V  L  M  Q  A  I  S  L  F  S  P  D  R  P  G  Y  L  Q  H  359
1381  GGCGTGGTTGACCAGCTGCAGGAGCAATTCGCCATTACTCTGAAGTCTTACATTGAAACC
       P  V  V  D  Q  L  Q  E  Q  F  A  I  T  L  K  S  Y  I  E  C  379
1441  AATCGGCCGCAGCCTCCATAGGTTGTTGTTCCTGAAGATCATCTATGTTGAGCTGAG
       N  R  P  Q  P  A  H  R  F  L  F  L  K  I  M  A  M  L  T  E  399
1501  GTCCGCAGCATCAATGCTGAGCACACGCAGCGGCTGCTGCGCATCCAGGACATACATCCC
       L  P  S  I  N  A  Q  H  T  Q  R  L  L  R  I  Q  D  I  H  P  419
1561  TTTGCTAGCGCCCTCATGGAGGAGTTGTTCGGCATCACAGGTAGCTGAGCGGCGCCTTT
       F  A  T  P  L  M  Q  E  L  F  G  I  T  G  S  *                 438
1621  GGGTGAGACTTCGGAGAGGCAGCAGACCCAGAGCCCTCTGAGCTGCTACTCCTTGGCTA
1681  AGACAGATGGACACTGCCAAGAGCCGACAATGCCCTGCTGGCCTGTCTCCCTAGGGAATT
1741  CCTGCTATGACAGCTGGCTAGCATTCCTCAGGAAGGACATGGGTGCCCCGACGTCCACT
1801  TCAGTCTGTAGGGAGTGAAGCCACAGACTCTTACGTGGAGAGTGCACTGACTTTAGGTC
1861  AGGACCATCAGAGAGGCAAGGTTGCCCTTTCCTTTTAAAAGGCCTTTGTCTCTGTAGA
1921  AATCCCTCAGATCCCACTAAAGTGTCAAGGTGTGGAAGGGACCAAGTGACAAGATAGG
1981  CCATCTGGGTTCTATGCCACATACCACGTTTGTTCGCTTCTGAGTTTTTCATTGCT
2041  ACCTCTAATAATGTCTGTCCCACTTGCCACTCGTTCCCCTCTTGTGAGTTGGTTTG
2101  TGGGCTCCAGGCCTGTACTCATCGGCAGGTGCATGAGTATCTCTAG
```

Figure 1A

B

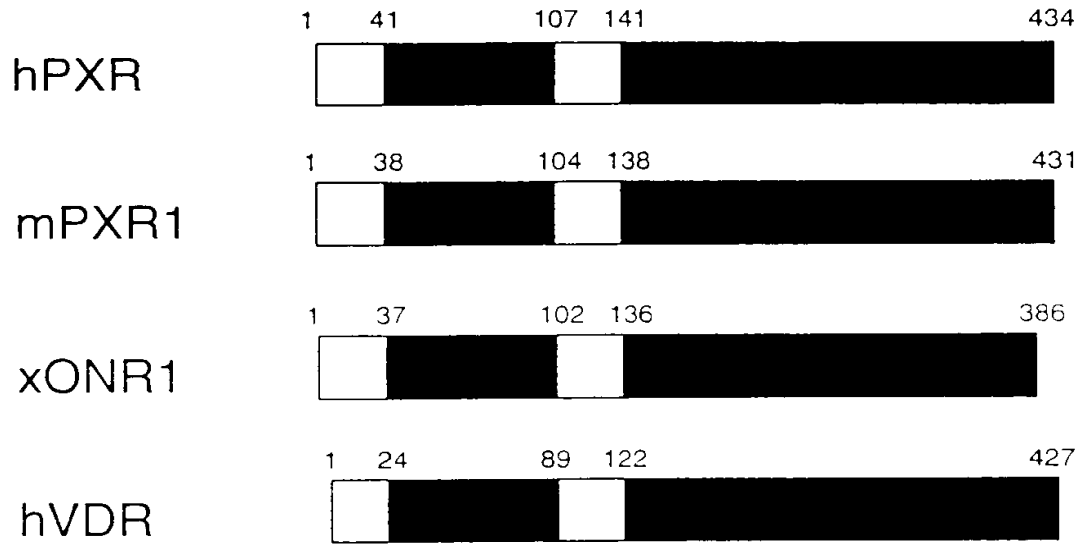

1
41
107
141
434
hPXR
1
38
104
138
431
mPXR1
1
37
102
136
386
xONR1
1
24
89
122
427
hVDR

Figure 1B

C

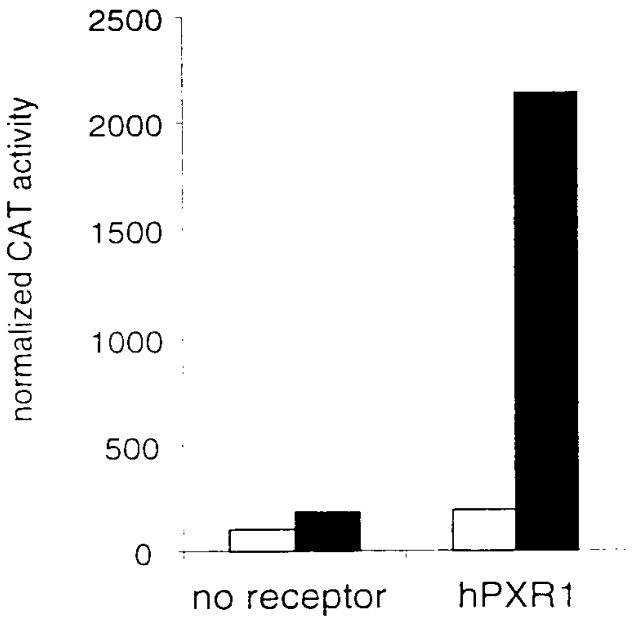

2500
2000
1500
1000
500
0
normalized CAT activity
no receptor
hPXR1

Figure 1C

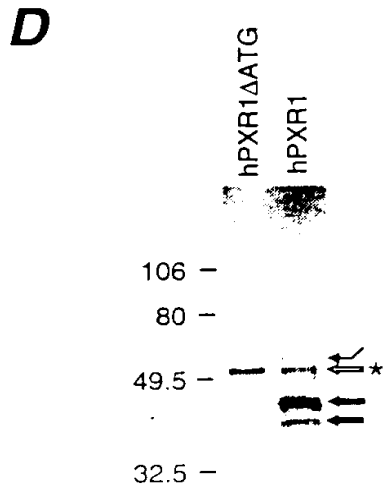


Figure 1D


heart
brain
placenta
lung
liver
skeletal muscle
kidney
pancreas
spleen
thymus
prostate
testis
ovary
small intestine
colon
PBL
9.5
7.5
4.4
2.4
1.4

Figure 2

A

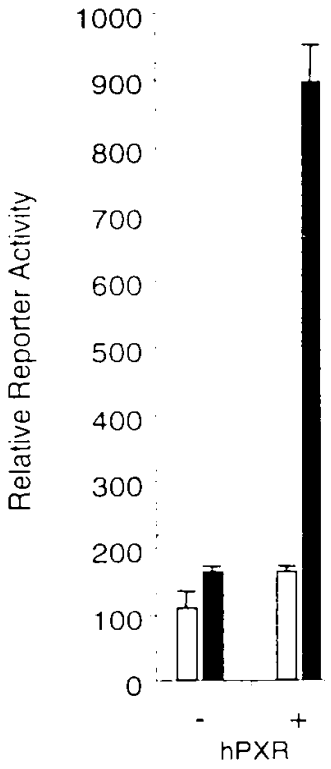

Relative Reporter Activity
1000
900
800
700
600
500
400
300
200
100
0
-
+
hPXR

Figure 3A

B

CYP3A4 IR6	ata **TGAACT** caaagg **AGGTCA** gtg <----- ----->
CYP3A4 IR6 m1	ata **TGTTCT** caaagg **AGAACA** gtg <-xx-- --xx->
CYP3A4 IR6 m2	ata **ACAACT** caaagg **AGGTCA** gtg xx---- ----->
CYP3A1 DR3	aga **TGAACT** tca **TGAACT** gtc <----- <-----

C

Figures 3B and 3C

A

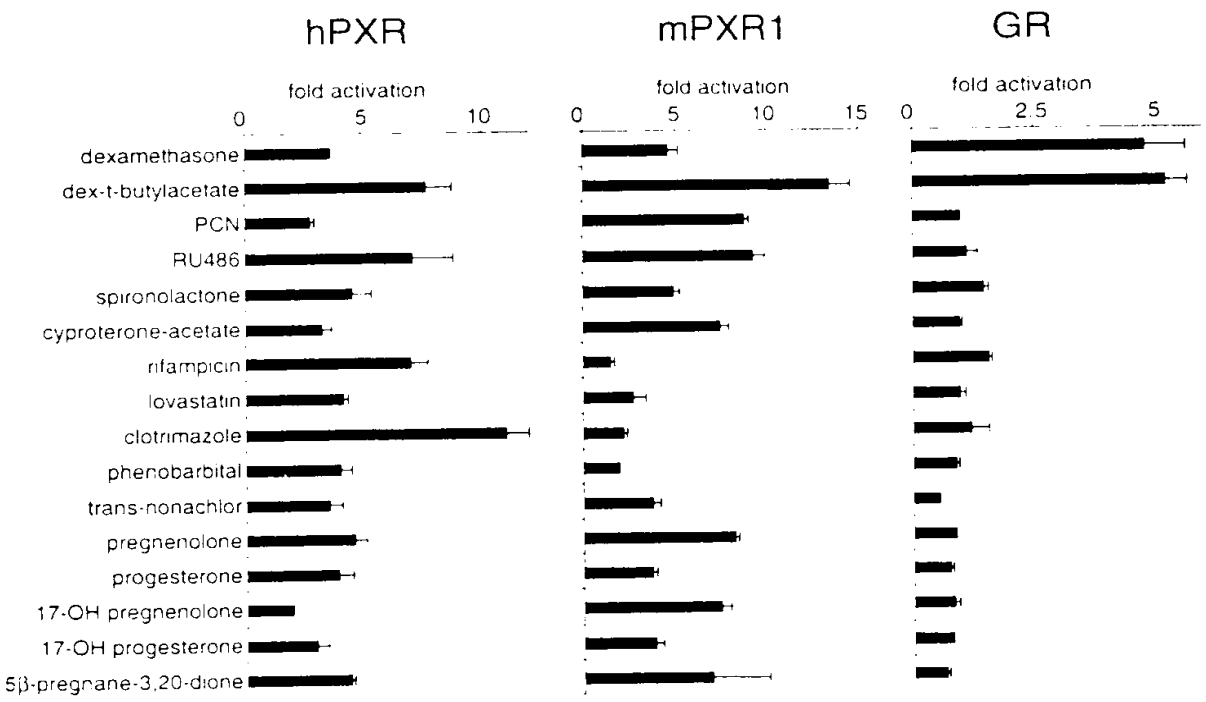

hPXR
mPXR1
GR
fold activation
0
5
10
15
2.5
dexamethasone
dex-t-butylacetate
PCN
RU486
spironolactone
cyproterone-acetate
rifampicin
lovastatin
clotrimazole
phenobarbital
trans-nonachlor
pregnenolone
progesterone
17-OH pregnenolone
17-OH progesterone
5β-pregnane-3,20-dione

Figure 4A

B

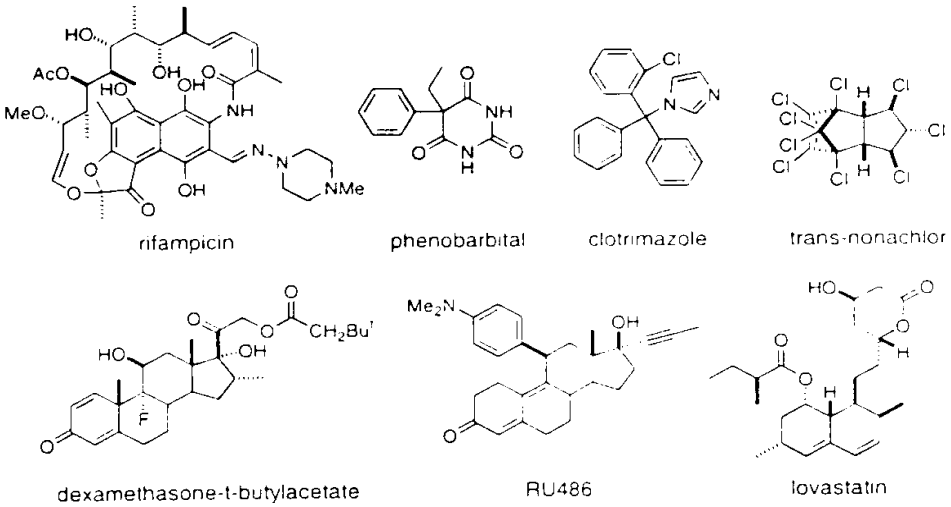

rifampicin
phenobarbital
clotrimazole
trans-nonachlor
dexamethasone-t-butylacetate
RU486
lovastatin

Figure 4B

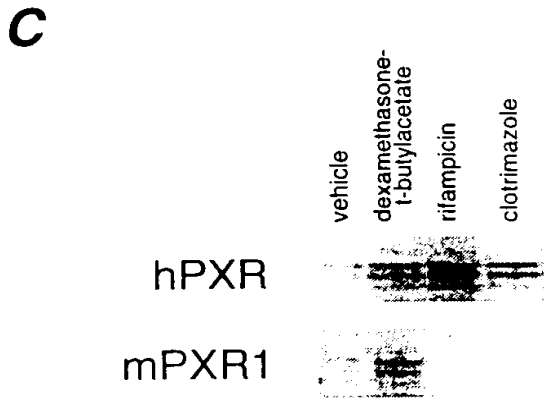
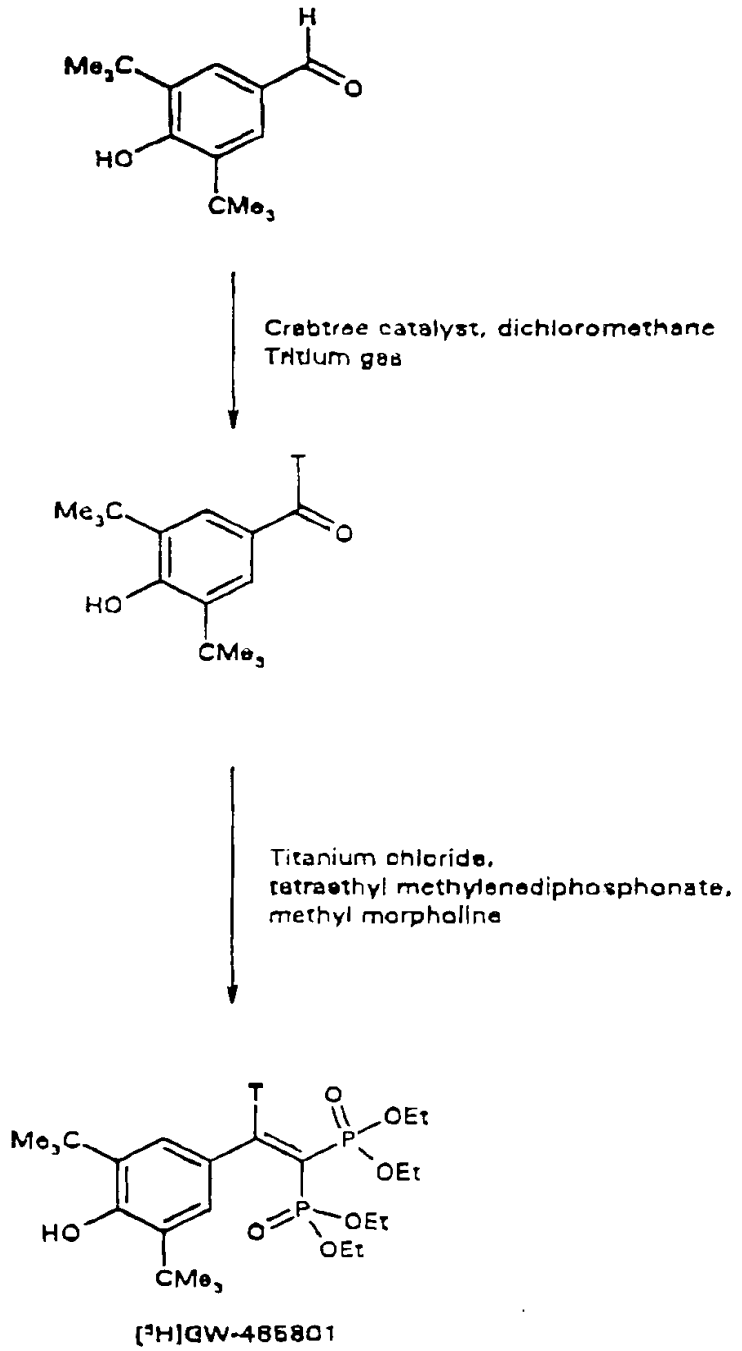

C
vehicle
dexamethasone-
t-butylacetate
rifampicin
clotrimazole
hPXR
mPXR1

Figure 4C

Figure 5

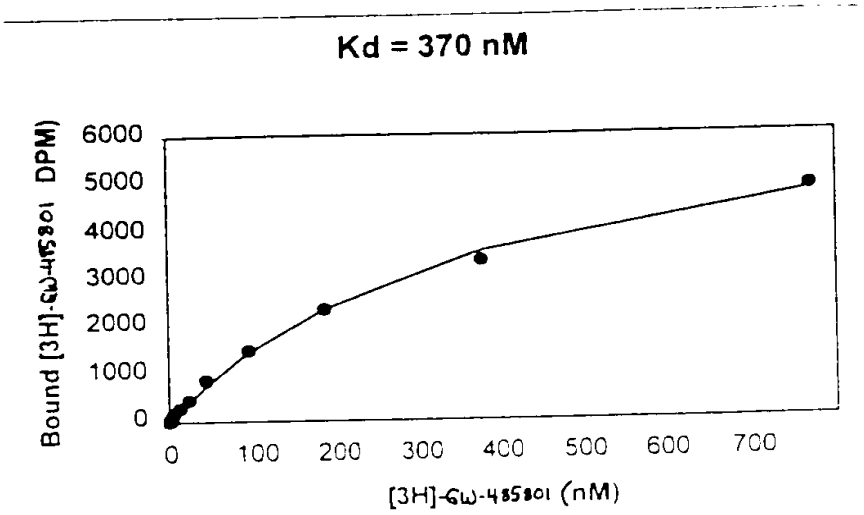
The Preparation of [^{3}H]GW-485801

1. REACTION SCHEME



[^{3}H]GW-485801

Figure 6


Kd = 370 nM
Bound [3H]-GW-485801 DPM)
6000
5000
4000
3000
2000
1000
0
0
100
200
300
400
500
600
700
[3H]-GW-485801 (nM)